REMARKS

Claims 3-19 are pending in the application. Claims 4, 7, 9, 18, and 19 are withdrawn as being drawn to non-elected inventions. Claims 3, 5, 6, 8, and 10-17 are under consideration. Claim 3 has been amended to further clarify the intended subject matter of the claimed invention. Entry of this amendment is respectfully requested. Applicants reserve the right to prosecute non-elected subject matter in subsequent divisional applications.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 3, 5, 6, 8, and 10-17 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite (Office Action, page 4). In particular, it was asserted that the term, "biologically-active fragment" is indefinite because "it is not clear what activities are bestowed upon these designated fragments described by this term." Applicants do not concede to the Patent Office position; however, in the interest of expediting prosecution, claim 3 has been amended to remove the recitation of biologically-active fragments. Therefore, withdrawal of the rejection of claim 3 and its dependent claims under 35 U.S.C. § 112, second paragraph, is respectfully requested.

Enablement Rejections under 35 U.S.C. § 112, first paragraph

Claims 3, 5, 6, 8, and 10-17 are rejected for allegedly failing to meet the requirements of 35 U.S.C. § 112, first paragraph, on the grounds that the specification does not provide an enabling disclosure commensurate in scope with the claims (Office Action page 4). In particular, the Office Action alleges that "[t]he specification discloses only the structural features of SEQ ID NO:1 (polypeptide) and its corresponding antibodies" (Office Action, page 4). Although Applicants do not concede to the Patent Office position, in the interest of expediting prosecution, claim 3 has been amended to recite "[a]n isolated antibody which specifically binds to an isolated polypeptide comprising an amino acid sequence of SEQ ID NO:1." The claims no longer recite fragments or variants of SEQ ID NO:1. Therefore, withdrawal of the enablement rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Written Description Rejections under 35 U.S.C. § 112, first paragraph

Claims 3, 5, 6, 8, and 10-17 have been rejected under the first paragraph of 35 U.S.C. 112 for alleged lack of an adequate written description. Although Applicants do not concede to the Patent Office position, in the interest of expediting prosecution, claim 3 has been amended such that it no longer recites fragments or variants of SEQ ID NO:1. Therefore, withdrawal of the written description rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Rejections under 35 U.S.C. § 101 and § 112

Claims 3, 5, 6, 8, and 10-17 are rejected under 35 U.S.C. § 101 and § 112 because the claimed invention is allegedly "not supported by either a specific and substantial asserted utility or a well established utility," and one skilled in the art, therefore, would not know how to use the claimed invention (Office Action, page 6). Applicants traverse the rejections for the reasons already made of record in the response to the Office Action of September 30, 2002, the Declaration of Mr. Furness, and on the following grounds.

A. Introduction

The Office Action states that "[t]he substantial likelihood that a protein is functionally related to another polypeptide is not sufficient to base the utility of an unknown protein and give merit to its use [sic] toxicology screening" (Office Action, page 7). Applicants strongly disagree. Nothing in the law requires Applicants to prove biological function, and the Examiner does not point to anything in the law suggesting such a requirement. Indeed, the only law on point is to the contrary: it is settled law -- and the Examiner does not rebut this -- that how an invention works (that is, its function) is utterly irrelevant to the utility analysis.

In this case, Applicants have identified the claimed polypeptide by association in a defined and narrow group: annexin binding proteins as well as expressed human polypeptides. As demonstrated below and in responses to previous Office Actions and the Furness Declaration, because annexin binding proteins as well as expressed human polypeptides are predominantly useful, Applicants can

state with great confidence that the claimed invention is useful. How the invention actually works is utterly irrelevant to the analysis.

B. Responses to Specific Arguments by Examiner

1. Biological function is irrelevant to utility

Applicants have demonstrated a utility for the claimed antibodies irrespective of whether or not a person would wish to perform additional experimentation to further assess biological function. The fact that additional experimentation could be performed to determine the functionality of the SEQ ID NO:1 polypeptide does not preclude, and is in fact irrelevant to, the actual utility of the invention. That utility exists today regardless of the specific function of the SEQ ID NO:1 polypeptide.

2. Use of claimed invention in toxicology testing and drug screening

The Examiner alleges that "toxicology testing and drug discovery are not disclosed in the specification as originally filed" (Office Action, page 7). However, well established uses, such as toxicology testing and drug screening, need not be explicitly described in the Specification. See the Furness Declaration at ¶¶ 10-12 for a discussion of the well-known use of 2D-PAGE maps in toxicology testing and drug screening.

For example, the Specification teaches that the polynucleotide sequences disclosed therein, including the polynucleotides encoding the SEQ ID NO:1 polypeptide, are useful as probes in chip based technologies which can be used "for the detection and/or quantification of nucleic acid or protein" (Specification at p. 20, lines 1-5). The Specification also discloses that the SEQ ID NO:1 polypeptide is useful in other protein expression detection technologies. The Specification states that "[a] variety of protocols for detecting and measuring the expression of NABP-1, using either polyclonal or monoclonal antibodies specific for the protein are known in the art. Examples include enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (RIA), and fluorescence activated cell sorting (FACS). A two-site, monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two non-interfering epitopes on NABP-1 is preferred, but a competitive binding assay may be employed." (Specification at p. 20, lines 11-15).

In addition, the Specification discloses using the SEQ ID NO:1 polypeptide and the antibody to the SEQ ID :NO:1 polypeptide in drug screening techniques (Specification at, e.g., page 36, lines 1-17).

> In another embodiment of the invention, NABP-1, its catalytic or immunogenic fragments or oligopeptides thereof, can be used for screening libraries of compounds in any of a variety of drug screening techniques. The fragment employed in such screening may be free in solution, affixed to a solid support, borne on a cell surface, or located intracellularly. The formation of binding complexes, between NABP-1 and the agent being tested, may be measured.
>
> Another technique for drug screening which may be used provides for high throughput screening of compounds having suitable binding affinity to the protein of interest as described in published PCT application WO84/03564. In this method, as applied to NABP-1 large numbers of different small test compounds are synthesized on a solid substrate, such as plastic pins or some other surface. The test compounds are reacted with NABP-1, or fragments thereof, and washed. Bound NABP-1 is then detected by methods well known in the art. Purified NABP-1 can also be coated directly onto plates for use in the aforementioned drug screening techniques. Alternatively, non-neutralizing antibodies can be used to capture the peptide and immobilize it on a solid support.
>
> In another embodiment, one may use competitive drug screening assays in which neutralizing antibodies capable of binding NABP-1 specifically compete with a test compound for binding NABP-1. In this manner, the antibodies can be used to detect the presence of any peptide which shares one or more antigenic determinants with NABP-1.

The Examiner states, on page 8 of the Office Action, that the specification does not convey to a person of ordinary skill that the invention could be used in protein expression monitoring for anything other than research on the claimed invention. This argument amounts to nothing more than the Examiner's disagreement with the Furness declaration (which purports therefore to substitute the Examiner's judgment for that of Applicants' expert) and Applicants' assertions about the knowledge of a person of ordinary skill. The Examiner must accept the Applicants' assertions to be true. The Exáminer is, moreover, wrong on the facts because Applicants demonstrate that the claimed invention can be used in gene and protein expression monitoring to study questions completely independent from characterizing the polypeptides. For example, the claimed methods could be used to determine whether a drug is likely to have toxic effects.

3. Irrelevance of differential expression to utility in toxicology testing

The Examiner argues on pages 7-8 of the Office Action that the Specification does not disclose whether the polypeptides are differentially expressed in different cells or tissues. This is irrelevant. Applicants need not demonstrate whether the polypeptides are differentially expressed, only whether the polypeptides are useful. The claimed antibodies are useful whether or not the SEQ ID NO:1 polypeptide is differentially expressed in any cells or tissues.

4. Utility of all expressed polynucleotides or polypeptides in toxicology testing

The Examiner argues on page 8 of the Office Action that "[n]one of the utilities identified by Applicants, i.e. toxicology testing, drug discover, disease diagnosis, have been demonstrated to be specific to SEQ ID NO:1." The Examiner does not point to any law, however, that says a utility that is shared by a large class is somehow not a utility. If all of the class of expressed human polypeptides can be so used, then they all have utility. The issue is, once again, whether the polypeptides has any utility, not whether other compounds have a similar utility. Nothing in the law says that an invention must have a "unique" utility. Indeed, the whole notion of "well-established" utilities PRESUPPOSES that many different inventions can have the exact same utility (if the Examiner's argument were correct, there could never be a well-established utility, because you could always find a generic group with the same utility!).

It is true that just about any expressed human polypeptide will have use as a toxicology control, but Applicants need not argue this for the purposes of this case. Applicants argue only that this particular claimed invention could be so used, and has provided the declaration of Furness to back this up. The Examiner is completely wrong to characterize Applicants' argument regarding utility as somehow requiring the person using the invention to do further research to identify biological function. The point is not whether the SEQ ID NO:1 polypeptide is, in any given toxicology test, differentially expressed. The point is that the invention provides a useful measuring stick regardless of whether there is or is not differential expression. That makes the invention useful today, in the real-world, for real purposes having nothing to do with further characterization of the invention itself.

5. Antibodies to the SEQ ID NO:1 polypeptide have utility regardless of any disease correlation

The Examiner further asserts that in order for the claimed antibodies to be useful in diagnosis of a disease, there must be a well established or disclosed correlation between the SEQ ID NO:1 polypeptide and a disease or disorder (Final Office Action, p. 8). This is not true. Applicants need not demonstrate whether the SEQ ID NO:1 polypeptide is associated with disease, only whether the claimed antibodies are useful. The claimed antibodies are useful whether or not the SEQ ID NO:1 polypeptide is associated with disease. Such antibodies have utility in protein expression monitoring applications, e.g., in the use of two-dimensional polyacrylamide gel electrophoresis and western blot analysis of tissue samples in drug development and in toxicity testing. Each sequence has a unique and specific utility in that it records the expression level of a unique gene or protein. This is a substantial, "real world" utility in that one of ordinary skill in the art would know how to use the claimed antibodies without any further experimentation.

If a drug candidate, targeted to a polypeptide other than the SEQ ID NO:1 polypeptide, alters expression of the SEQ ID NO:1 polypeptide, that drug candidate is considered to have an undesirable side effect. As Mr. Furness explains in his declaration, good drugs "have strong effects on a specific biological target and minimal effects on all other biological targets" (Furness Declaration, ¶ 10). Disruption of the expression of a polypeptide which is not the target of a drug candidate is, therefore, an undesired side effect of that drug candidate. Measuring the expression level of the SEQ ID NO:1 polypeptide, such as during a toxicology test of a drug candidate targeted to another polypeptide, would **not** require knowledge of the biological function or disease association of the SEQ ID NO:1 polypeptide, as the Office Action would have it.

C. The Office Action is Based on Flawed Assumptions about the Legal Standard for Utility

In the face of Applicants' demonstration of numerous disclosed and well-established utilities for the claimed antibodies, the Office Action does not offer any facts or sound scientific reasoning as would be required to overcome the presumption of utility that must be attributed to the claimed invention as a matter of law.

Also pertinent are the explanations in the Furness Declaration (at, e.g., ¶¶ 10-12) regarding why persons skilled in the art, who read the Hillman '801 application on July 31, 1997 (the Hillman '801 application is the priority application, U.S. Serial No. 08/903,801, on which the instant application is based), would have (a) concluded that the SEQ ID NO:1 polypeptide and the antibody to the SEQ ID NO:1 polypeptide would be useful in 2-D PAGE analyses for the development of new drugs and monitoring the activities of drugs for such purposes as evaluating their efficacy and toxicity (b) requested specifically that any 2D-PAGE map that was being used for such purposes contain the SEQ ID NO:1 polypeptide sequence, and (c) requested that the antibody to the SEQ ID NO:1 polypeptide be used for detection of the SEQ ID NO:1 polypeptide in protein expression monitoring studies. These explanations show, beyond any doubt, that the claimed antibodies are highly useful tools in gene and protein expression monitoring applications used in connection with the development of drugs for treating cancer, immune disorders, or neurological disorders.

The Examiner has not and cannot provide **any** evidence tending to show that a person of ordinary skill in the art could not achieve the disclosed utilities, or indeed that any experimentation whatsoever would be required to put the claimed invention to beneficial use. And the Office Action utterly fails to address the Applicants' overwhelming evidence demonstrating not only that persons of ordinary skill in the art recognize the utility of inventions such as those claimed, but also that the likelihood that the claimed invention would achieve those utilities is far beyond substantial.

Apart from ignoring the presumption of utility and the Examiner's burden to overcome it, the entirety of the Office Action ultimately is based on two flawed assumptions. They are:

i. the claimed invention cannot be proven to be useful until the biological roles or functions of the polypeptides also are proven; and

ii. assignment to a family whose members are known to be useful does not establish utility unless the members share a single, common utility.

These assumptions are incorrect.[1]

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[1] It is respectfully submitted that the entirety of the Examiner's alleged rebuttal of Applicants' arguments and reasoning in the Office Action are based on these incorrect assumptions. Nevertheless,

1. The precise biological role or function of an expressed polynucleotide or protein is not required to demonstrate utility

Rather than responding to Applicants' evidence demonstrating utility, the Examiner attempts to dismiss it altogether by arguing that the disclosed and well-established utilities for the SEQ ID NO:1 polypeptide are not specific, substantial, and credible utilities (Office Action at page 6). The Examiner is incorrect both as a matter of law and as a matter of fact.

The basis of the Examiner's argument is that, without information as to the precise biological role of the claimed invention, the claimed invention's utility is not sufficiently specific. According to the Examiner, it is not enough that a person of ordinary skill in the art could use and, in fact, would want to use the SEQ ID NO:1 polypeptide and the antibody to the SEQ ID NO:1 polypeptide either individually or in a 2D-PAGE map to monitor the expression of genes and proteins for such applications as the evaluation of a drug's efficacy and toxicity.

It may be that such detailed information on biological function is necessary to satisfy the requirements for publication in some technical journals, but it is not necessary to satisfy the requirements for obtaining a United States patent. The relevant question is not, as the Examiner would have it, whether it is known how or why the invention works, *In re Cortwright*, 165 F.3d 1353, 1359 (Fed. Cir. 1999), but rather whether the invention provides an "identifiable benefit" in presently available form. *Juicy Whip Inc.* v. *Orange Bang Inc.*, 185 F.3d 1364, 1366 (Fed. Cir. 1999)[2]. If the benefit exists, and there is a substantial likelihood the invention provides the benefit, it is useful. There can be

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to the extent that Applicants do not specifically rebut these points on a line-by-line basis, this is not to be construed as acquiescence to their veracity, and Applicants do not waive the right to rebut them individually at any later point in the proceedings.

[2] *Juicy Whip* states:
An invention is "useful" under section 101 if it is capable of providing some identifiable benefit. See *Brenner v. Manson*, 383 U.S. 519, 534 [148 USPQ 689] (1966); *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 [24 USPQ2d 1401] (Fed. Cir. 1992) ("to violate Section 101 the claimed device must be totally incapable of achieving a useful result"); *Fuller v. Berger*, 120 F. 274, 275 (7th Cir. 1903) (test for utility is whether invention "is incapable of serving any beneficial end").

no doubt, particularly in view of the Furness Declaration (at, *e.g.*, ¶¶ 10-13), that the present invention easily meets this test.

The threshold for determining whether an invention produces an identifiable benefit is low. *Juicy Whip*, 185 F.3d at 1366. Only those utilities that are so nebulous that a person of ordinary skill in the art would not know how to achieve an identifiable benefit and, at least according to the PTO guidelines, so-called "throwaway" utilities that are not directed to a person of ordinary skill in the art at all, do not meet the statutory requirement of utility. Utility Examination Guidelines, 66 Fed. Reg. 1092 (Jan. 5, 2001).

Knowledge of the biological function or role of a biological molecule has never been required to show real-world benefit. In its most recent explanation of its own utility guidelines, the PTO acknowledged so much (66 F.R. at 1095):

> [T]he utility of a claimed DNA does not necessarily depend on the function of the encoded gene product. A claimed DNA may have specific and substantial utility because, *e.g.*, it hybridizes near a disease-associated gene or it has gene-regulating activity.

Biological role or function is, instead, merely one factor that can be relevant in demonstrating whether there is a "substantial likelihood" a claimed invention can achieve the identified benefits. It may be particularly helpful in those cases where it is necessary to prove that the identifiable benefit of one biological composition can be imputed to another. In these cases, see, *e.g.*, *In re Brana*, 51 F.3d 1560, 1566; 34 USPQ2d 1436 (Fed. Cir. 1995), because there is no direct evidence that the biological composition can achieve any given utility, knowledge of biological function can be used to prove a "substantial likelihood' of utility indirectly, by association. Biological function serves as a link between a compound whose utility otherwise would be unknown and another compound having known utility. If, for example, a prior art biological composition is known to be a target in the treatment of disease, one way the applicant can prove utility is by demonstrating that the claimed invention is substantially likely to share the utility for disease treatment because it also shares a biological role with the prior art composition.

But in other cases, such as this one, proof of biological function is not necessary. In those cases, the evidence already is sufficient to show that there is a substantial likelihood that the claimed

invention produces the alleged benefit. The claimed invention has a known utility whether or not it can be linked (through biological function) with some other composition.

By implicitly requiring knowledge of biological function for any claimed nucleic acid or protein, the Examiner has, contrary to law, elevated what has long been acknowledged to be an evidentiary factor into an absolute requirement of utility. Rather than looking to the biological role or function of the claimed invention, the Examiner should have looked first to the benefits it is alleged to provide.

2. Assignment to a family whose members are useful establishes utility

The Examiner cannot properly impose a "common utility" requirement with respect to the annexin binding protein family and the family of expressed human polypeptides to which NABP-1 belongs. The Examiner's attempt to do so, if permitted to succeed, would improperly raise the threshold of patentable utility for biotechnological inventions to a point above that of other classes of inventions.

Similarities between NABP-1 and rat annexin V binding protein (g1514949) are described in the specification, for example, at page 11, lines 23-33, and depicted in Figures 2 and 3. The specification points out the roles of annexins in regulation of phospholipase A2, anticoagulant activity, cellular exocytosis, membrane trafficking, cytoskeletal organization, phosphohydrolase activity, cell proliferation, and calcium channel activity (Specification at pages 1-2). Members of the annexin family have been implicated in cancer, neurodegenerative diseases, autoimmune diseases, and inflammatory bowel diseases (enclosed references of Bastian (1997) Cell. Mol. Life Sci. 53:554-556; Eberhard et al. (1994) Am. J. Pathol. 145:640-649; and Gerke and Moss (2002) Physiol. Rev. 82:331-371). Annexin V, in particular, has been found to be useful as a marker of apoptosis to monitor the changes in phospholipid distribution that accompany cell death (enclosed references of Blankenberg et al. (1998) Proc. Natl. Acad. Sci. U.S.A. 95:6349-6354 and Blankenberg et al. (2000) Eur. J. Nucl. Med. 27:359-367). Annexin V is also useful in radionuclide imaging for diagnosis of stroke, neurodegenerative diseases, inflammatory diseases, myocardial ischemia, myelodysplastic disorders, organ transplantation, and cancer.

Furthermore, this is not a case in which biological function is necessary to provide a link between the claimed invention on the one hand, and a compound of known utility on the other. Given that the claimed invention is disclosed in the Hillman '801 to be useful as a tool in a number of gene and protein expression monitoring applications that were well-known at the time of the filing of the application in connection with the development of drugs and the monitoring of the activity of drugs, the precise biological function of the SEQ ID NO:1 polypeptide is superfluous information for the purposes of establishing utility.

The uncontested fact that the claimed invention already has a disclosed use as a tool in then available technology (such as 2D-PAGE maps) distinguishes it from those few claimed inventions found not to have utility. In each of those cases, unlike this one, the person of ordinary skill in the art was left to guess whether the claimed invention could be used to produce an identifiable benefit.

Brenner v. *Manson*, 383 U.S. 519, 532, 534-35 (1966) concerns a narrow exception to the general rule that inventions are useful. It holds that where the assertion of utility for the claimed invention is made by association with a group including useful members, the group may not include so many useless members that there would be less than a substantial likelihood that the claimed invention is in fact one of the useful members of the group. In *Brenner*, the claimed invention was a process for making a synthetic steroid. Some steroids are useful, but most are not. While the claimed process in *Brenner* produced a composition that bore homology to some useful steroids, antitumor agents, it also bore structural homology to a substantial number of steroids having no utility at all. There was no evidence that could show, by substantial likelihood, that the claimed invention would produce the benefits of the small subset of useful steroids. It was entirely possible, and indeed likely, that the claimed invention was just as useless as the majority of steroids.

In *Brenner*, the steroid was not disclosed in the application for a patent to be useful in its then-present form. Here, in contrast, the polynucleotide detected by the claimed methods is an expressed polynucleotide that was disclosed to be useful in the Hillman '801 for many known applications involving gene and protein expression monitoring analysis. Its utility is not a matter of guesswork. It is not a random DNA or polypeptide sequence that might or might not be useful as a scientific tool. Unlike the steroid in *Brenner*, the utility of the invention claimed here is not grounded

upon being structurally analogous to a molecule which belongs to a class of molecules containing a significant number of useless compositions.[3]

And, the utilities disclosed in the application are for purposes other than just studying the claimed invention itself, *Brenner*, 383 U.S. at 535, i.e., for other (non self-referential) uses such as to ascertain the toxic potential of a drug candidate and to study the efficacy of a proposed drug. Indeed, in view of the Furness Declaration (at, e.g., ¶ 12), the evidence shows that persons skilled in the art on July 31, 1997, who read the Hillman '801, would have believed the SEQ ID NO:1 polypeptide and the antibody to the SEQ ID :NO:1 polypeptide to be so useful that they would request them to be included as probes in 2D-PAGE maps for conducting gene and protein expression analyses in association with identifying drugs for treating cancer, immune disorders, or neurological disorders.

Accordingly, in this case, biological function is in fact superfluous information for the purposes of demonstrating utility. Here, the claimed invention is more than "substantially likely" to be useful, in a way that is utterly independent of knowledge of precise biological function, as the Furness Declaration and other evidence presented by the Applicants demonstrates. Given that the claimed invention has disclosed and well-established utilities, the Applicants need not demonstrate utility by imputation.

In the end, the Examiner has failed to recognize that new technologies, such as those involving the use of 2D-PAGE maps, to conduct gene and protein expression analyses, have made useful biological molecules that might not otherwise have been useful in the past. *See Brenner*, 383 U.S. at 536. Technology has now advanced well beyond the point that a person of ordinary skill in the art would have to guess whether a newly discovered expressed polynucleotide or protein could be usefully employed without further research. It has created a need for new tools, such as the SEQ ID NO:1 polypeptide and the antibody to the SEQ ID :NO:1 polypeptide, that provide, and have been providing for some time now, unquestioned commercial and scientific benefits, and **real-world benefits** to the public by enabling faster, cheaper and safer drug discovery processes. The Examiner is obliged, by law, to recognize this reality.

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[3] While not necessary to reverse the Examiner's rejections, it is appropriate to point out that because the SEQ ID NO:1 polypeptide is an expressed human polypeptide, it is highly more likely than not that it belongs to the class of molecules that have been pre-selected by nature to be useful.

D. To the extent the rejection of the patented invention under 35 U.S.C. § 112, first paragraph, is based on the improper rejection for lack of utility under 35 U.S.C. § 101, it must be reversed.

The rejection set forth in the Office Action is based on the assertions discussed above, i.e., that the claimed invention lacks patentable utility. To the extent that the rejection under § 112, first paragraph, is based on the improper allegation of lack of patentable utility under § 101, it fails for the same reasons. Withdrawal of the rejections of the claims under 35 U.S.C. §101 and §112 is therefore respectfully requested.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact Applicants' Attorney at (650) 855-0555.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108.**

Respectfully submitted,

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3. (Twice Amended) An isolated antibody which specifically binds to an isolated polypeptide comprising an amino acid sequence of SEQ ID NO:1.

4. (As Once Amended) A method for a diagnostic test for a condition or disease associated with the expression of NABP-1 in a biological sample, the method comprising:

a) combining the biological sample with an antibody of claim 3, under conditions suitable for the antibody to bind the polypeptide and form an antibody: polypeptide complex; and

b) detecting the complex, wherein the presence of the complex correlates with the presence of the polypeptide in the biological sample.

5. The antibody of claim 3, wherein the antibody is:

(a) a chimeric antibody;

(b) a single chain antibody;

(c) a Fab fragment;

(d) a $F(ab')_2$ fragment; or

(e) a humanized antibody.

6. A composition comprising an antibody of claim 3 and an acceptable excipient.

7. A method of diagnosing a condition or disease associated with the expression of NABP-1 in a subject, comprising administering to said subject an effective amount of the composition of claim 6.

8. A composition of claim 6, wherein the antibody is labeled.

9. A method of diagnosing a condition or disease associated with the expression of NABP-1 in a subject, comprising administering to said subject an effective amount of the composition of claim 8.

10. (As Once Amended) A method of preparing a polyclonal antibody with the specificity of the antibody of claim 3, the method comprising:

a) immunizing an animal with a polypeptide consisting of an amino acid sequence of SEQ ID NO:1, or an immunogenic fragment thereof, under conditions to elicit an antibody response;

b) isolating antibodies from said animal; and

c) screening the isolated antibodies with the polypeptide, thereby identifying a polyclonal antibody which binds specifically to a polypeptide comprising an amino acid sequence of SEQ ID NO:1.

11. An antibody produced by a method of claim 10.

12. A composition comprising the antibody of claim 11 and a suitable carrier.

13. (As Once Amended) A method of making a monoclonal antibody with the specificity of the antibody of claim 3 comprising:

a) immunizing an animal with a polypeptide consisting of an amino acid sequence of SEQ ID NO:1, or an immunogenic fragment thereof, under conditions to elicit an antibody response;

b) isolating antibody producing cells from the animal;

c) fusing the antibody producing cells with immortalized cells to form monoclonal antibody-producing hybridoma cells;

d) culturing the hybridoma cells; and

e) isolating from the culture monoclonal antibody which binds specifically to a polypeptide comprising an amino acid sequence of SEQ ID NO:1.

14. A monoclonal antibody produced by a method of claim 13.

15. A composition comprising the antibody of claim 14 and a suitable carrier.

16. The antibody of claim 3, wherein the antibody is produced by screening a Fab expression library.

17. The antibody of claim 3, wherein the antibody is produced by screening a recombinant immunoglobulin library.

18. (As Once Amended) A method for detecting a polypeptide comprising an amino acid sequence of SEQ ID NO:1 in a sample, the method comprising:

a) incubating the antibody of claim 3 with a sample under conditions to allow specific binding of the antibody and the polypeptide; and

b) detecting specific binding, wherein specific binding indicates the presence of a polypeptide comprising an amino acid sequence of SEQ ID NO:1 in the sample.

19. (As Once Amended) A method of purifying a polypeptide comprising an amino acid sequence of SEQ ID NO:1 from a sample, the method comprising:

a) incubating the antibody of claim 3 with a sample under conditions to allow specific binding of the antibody and the polypeptide; and

b) separating the antibody from the sample and obtaining the purified polypeptide comprising an amino acid sequence of SEQ ID NO:1.

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claim 3 has been amended as follows:

3. (Twice Amended) An isolated antibody which specifically binds to an isolated polypeptide [selected from the group consisting of:

a) a polypeptide] comprising an amino acid sequence of SEQ ID NO:1[, and

b) a polypeptide comprising a naturally-occurring amino acid sequence having at least 90% sequence identity to the sequence of SEQ ID NO:1.

c) a biologically-active fragment of a polypeptide having the amino acid sequence of SEQ ID NO:1, comprising at least 25 contiguous amino acid residues of SEQ ID NO:1, wherein the biologically-active fragment binds to annexin, and

d) an immunogenic fragment of a polypeptide having the amino acid sequence of SEQ ID NO:1 comprising at least 25 contiguous amino acid residues of SEQ ID NO:1].